UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,385	09/05/2003	Pragnya J. Desai	JJPR-0036	9589

23377 7590 01/05/2007

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,385	DESAI ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-29 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/05, 2/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 10/27/06 is acknowledged and has been entered.

2. Applicant's election without traverse insofar as the groups are directed to patentably distinct inventions, and with traverse of Group V (claim 30) wherein the modulator is an antagonist, in the said response is acknowledged.

Applicant's traversal is with regard to the five inventions encompassed by Group V: the different types of compounds have not been shown to fall into different search classes such that the search of different types of compounds, *i.e.,* inhibitor, activator, antagonist, agonist or inverse agonist, would be unduly burdensome, and in performing the claimed method for drug discovery, the property of the compound being tested is typically not known.

Applicant's argument is deemed persuasive by the Examiner.

Accordingly, claims 1-29 and 31 (non-elected groups I-IV and VI) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claim 30 is currently being examined.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration, *i.e.,* non-dated alterations to Inventor Dunford's zip code and to Inventor Leung's citizenship. See 37 CFR 1.52(c).

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

5. The disclosure is objected to because of the following informalities:

The use of the trademark FLASHPLATE has been noted in this application on page 16 at [0059]. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction(s) is/are required.

6. The references on page 1 of the information disclosure statement filed 4/22/05 have not been considered because they do not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It is noted by the Examiner that for each said patent, information has been provided in the English language that does not appear to correlate with the non-English patent as an abstract. In addition, the two references on pages 2 and 6, respectively, have not been considered because they have not been provided by Applicant.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 30 is rejected under 35 U.S.C. 103(a) as being obvious over US 2003/0133931 A1 in view of WO 02/056871 A2 (IDS reference), Arai *et al* (PNAS USA 1997, 94: 14495-14499) and Matsuura *et al* (J. Exp. Med. 1989, 170: 1421-1426).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

US 2003/0133931 A1 discloses a method of identifying compounds that modulate mammalian histamine H4 receptor (HH4R) protein activity, said method comprising combining a candidate HH4R modulator compound with a HH4R protein and a known HH4R ligand such as histamine *in vitro*, and measuring an effect of the candidate modulator on the function of the HH4R, such as wherein the candidate compound modulates inflammation or inflammatory responses such as mast cell activation. US 2003/0133931 A1 discloses that the assays used may be a simple "yes/no" assay to determine whether there is a change in the function or activity of the receptor protein, and that the assay may be made quantitative by comparing the function of a test sample with the receptor protein function in a standard sample. US 2003/0133931 A1 discloses that activation of mast cells causes the mast cells to subsequently undergo migration to a particular location, *i.e.*, chemotaxis, and/or to undergo de-granulation.

US 2003/0133931 A1 discloses that HH4R has been cloned and demonstrated to be expressed in a variety of cells, including but not limited to, leukocytes and mast cells. US 2003/0133931 A1 discloses that the HH4R is involved in the inflammatory response, and particularly involved in leukocyte recruitment to the site of inflammation, and that antagonists for this receptor are anti-inflammatory. US 2003/0133931 A1 discloses that modulators of such inflammation are useful for treatment of inflammatory responses. (especially claims, abstract, [0003], [0010]-[0012], [0022]).

US 2003/0133931 A1 does not disclose wherein the function of the test sample measured is mast cell chemotaxis in response to histamine.

WO 02/056871 A2 teaches a functional assay for the HH4R determines the ability of histamine to induce chemotaxis in eosinophils isolated from human blood, that the ability of potential antagonists to antagonize the ability of histaminergic ligands in promoting migration of eosinophils across a permeable membrane is studied (especially page 8 at lines 8-23). WO 02/056871 A2 teaches that histamine-induced chemotaxis (migration towards a chemoattractant) of human eosinophils appears to be mediated by the HH4R, and not by the HH3R, and therefore the HH4R receptor antagonists can prevent histamine-induced chemotaxis of human eosinophils.

Arai *et al* teach an assay for measuring chemotaxis of a lymphocyte cell line transfected with a G-coupled receptor using a transwell system (especially abstract and materials and methods at the "Chemotaxis Assay" section on page 14496 at column 1).

Matsuura *et al* teach an assay for measuring chemotaxis of mast cells using a modified Boyden chamber (especially introduction, materials and methods, page 1424 at the last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have identified antagonists of HH4R by measuring a function of HH4R protein such as mast cell activation, the measure of activation being mast cell chemotaxis in response to histamine as disclosed by US 2003/0133931 A1 by using a chemotaxis assay as taught by Matsuura *et al* or Arai *et al* that is compatible for use with mast cells, in a manner similar to that taught by WO 02/056871 A2 for measuring chemotaxis in eosinophils to identify potential antagonists of HH4R on another cell type important in inflammatory responses.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to identify antagonists by measuring a functional property such as chemotaxis of mast cells as disclosed by US 2003/0133931 A1, because US 2003/0133931 A1 discloses the importance of identifying antagonists of HH4R on mast cells for treatment of inflammatory reactions, WO 02/056871 A2 teaches the importance of identifying antagonists of HH4R on another cell type important in inflammatory reactions by measuring chemotaxis, and Arai *et al* and Matsuura *et al*

teach assays for measuring chemotaxis of white blood cells such as lymphocytes and mast cells.

9. Claim 30 is rejected under 35 U.S.C. 103(a) as being obvious over US 2003/0133931 A1 in view of Arai *et al* (PNAS USA 1997, 94: 14495-14499) and Matsuura *et al* (J. Exp. Med. 1989, 170: 1421-1426)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

US 2003/0133931 A1 discloses a method of identifying compounds that modulate mammalian histamine H4 receptor (HH4R) protein activity, said method comprising combining a candidate HH4R modulator compound with a HH4R protein and a known HH4R ligand such as histamine *in vitro*, and measuring an effect of the candidate modulator on the function of the HH4R, such as wherein the candidate compound modulates inflammation or inflammatory responses such as mast cell activation.
US 2003/0133931 A1 discloses that the assays used may be a simple "yes/no" assay to determine whether there is a change in the function or activity of the receptor protein, and that the assay may be made quantitative by comparing the function of a test sample with the receptor protein function in a standard sample. US 2003/0133931 A1 discloses that activation of mast cells causes the mast cells to subsequently undergo migration to a particular location, *i.e.,* chemotaxis and/or to undergo de-granulation.
US 2003/0133931 A1 discloses that HH4R has been cloned and demonstrated to be expressed in a variety of cells, including but not limited to, leukocytes and mast cells.
US 2003/0133931 A1 discloses that the HH4R is involved in the inflammatory response, and particularly involved in leukocyte recruitment to the site of inflammation, and that antagonists for this receptor are anti-inflammatory. US 2003/0133931 A1 discloses that modulators of such inflammation are useful for treatment of inflammatory responses. (especially claims, abstract, [0003], [0010]-[0012], [0022]).

US 2003/0133931 A1 does not disclose wherein the function of the test sample measured is mast cell chemotaxis in response to histamine.

Arai *et al* teach an assay for measuring chemotaxis of a lymphocyte cell line transfected with a G-coupled receptor using a transwell system (especially abstract and materials and methods at the "Chemotaxis Assay" section on page 14496 at column 1).

Matsuura *et al* teach an assay for measuring chemotaxis of mast cells using a modified Boyden chamber (especially introduction, materials and methods, page 1424 at the last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have identified antagonists of HH4R by measuring a function of HH4R protein such as mast cell activation that is mast cell chemotaxis in response to histamine as disclosed by US 2003/0133931 A1 by using a chemotaxis assay as taught by Matsuura *et al* or Arai *et al* that is compatible for use with mast cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to identify antagonists by measuring a functional property such as chemotaxis of mast cells as disclosed by US 2003/0133931 A1, because US 2003/0133931 A1 discloses the importance of identifying antagonists of HH4R on mast cells for treatment of inflammatory reactions, and Arai *et al* and Matsuura *et al* teach assays for measuring chemotaxis of white blood cells such as lymphocytes and mast cells.

10. Claim 30 is rejected under 35 U.S.C. 103(a) as being obvious over WO 01/92485 (IDS reference) in view of US Patent No. 5,000,936, Morse *et al* (J. Pharmac. Exp. Ther. 2001, 296(3) : 1058-1066, IDS reference), Arai *et al* (PNAS USA 1997, 94: 14495-14499) and Matsuura *et al* (J. Exp. Med. 1989, 170: 1421-1426).

WO 01/92485 teaches the cloning and expression of the mammalian HH4R, and a method of identifying compounds that modulate the HH4R protein activity by combining a test compound with the HH4R in the presence of a known HH4R ligand and measuring the function of the HH4R protein, such as for example, measuring an HH4R intracellular second messenger. WO 01/92485 teaches that histamine mediates inflammatory and allergic responses (especially page 2, claims 17-22, page 27 at lines 17-21 through page 28).

WO 01/92485 does not teach wherein the method involves measurement of activation of a cell that expresses endogenous HH4R such as a mast cell, said activation including chemotaxis.

US Patent No. 5,000,936 discloses that "allergy" has become synonymous with Type I hypersensitivity in which the reactions are dependent on the specific triggering of IgE-sensitized mast cell by antigen, resulting in the degranulation of mast cells and the release of pharmacological mediators of inflammation such as histamine. US Patent No. 5,000,936 discloses that the vasoactive amine histamine from mast cells and basophils increases vascular permeability and attracts polymorphs (*i.e.,* neutrophils, eosinophils, basophils) (especially column 1 at line 43 through column 2 at line 10).

Morse *et al* teach SP9144 (*i.e,* HH4R) has a very limited distribution, primarily in lymphoid tissues such as T cells, DC, monocytes, mast cells, neutrophils and eosinophils. Morse *et al* teach that expression of HH4R in immune system cells is potentially significant since histamine has been shown to exhibit activity at various types of leukocytes. Morse *et al* teach that their HH4R is essentially identical to the novel histamine receptor reported by Oda *et al* (especially page 1064 at the last paragraph, last two paragraphs of article).

Arai *et al* teach an assay for measuring chemotaxis of a lymphocyte cell line transfected with a G-coupled receptor using a transwell system (especially abstract and materials and methods at the "Chemotaxis Assay" section on page 14496 at column 1).

Matsuura *et al* teach an assay for measuring chemotaxis of mast cells using a modified Boyden chamber (especially introduction, materials and methods, page 1424 at the last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have identified an antagonist of HH4R using the method taught by WO 01/92485 of measuring a function such as activation of HH4R by assessing the function of the HH4R to histamine in the presence of a known HH4R ligand, by using mast cells that express HH4R endogenously as taught by Morse *et al*, in the presence of histamine taught by WO 01/92485 and disclosed by US Patent No. 5,000,936 to mediate inflammatory and allergic responses, using the assay taught by Arai *et al* or Matsuura *et al* that is suitable for measuring chemotaxis of leukocytes.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to identify antagonists of HH4R by measuring a function such as activation of HH4R in the presence of a ligand of HH4R such as histamine as disclosed by WO 01/92485 using a cell such as a mast cell that endogenously expresses HH4R on its surface as taught by Morse *et al*, said cell being important in the inflammatory type 1 hypersensitivity or allergic IgE response as disclosed by US Patent No. 5,000,936, and chemotaxis assays suitable for measuring chemotaxis of mast cells or other leukocytes being routine in the art as taught by Matsuura *et al* and Arai *et al*.

In addition, it was recognized in the prior art that chemotaxis, degranulation of mast cells, and activation of a second messenger in response to histamine receptor-ligand binding are indicators of mast cell function, specifically activation. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
December 19, 2006

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600